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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,742	12/28/2001	James G. Karras	ISPH-0623	8407

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EXAMINER	
GIBBS, TERRA C	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,742	KARRAS ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 2, 4-10 and 12-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicants Amendment filed December 4, 2003 and Applicants Remarks filed March 20, 2003.

Claims 3, 11, and 15-20 have been canceled. Claim 1 has been amended. A compound 8 to 50 nucleobases in length targeted to a 5'-untranslated region, a start codon region or a coding region of a nucleic acid molecule encoding macrophage inflammatory protein-3 (SEQ ID NO:3) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement on December 4, 2003.

Claims 1, 2, 4-10 and 12-14 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of a compound 8 to 50 nucleobases in length targeted to a 3'-untranslated region of a nucleic acid molecule encoding macrophage inflammatory protein-3 alpha (SEQ ID NO:3) is acknowledged. The traversal is on the ground(s) that MPEP 802.1 defines "independent" and "distinct" and by definition, the sequences recited in claim 1 cannot be "independent" or "distinct" because they all target and modulate the same single sequence, namely SEQ ID NO:3. Applicants further argue that in most cases, up to ten independent and distinct nucleotide sequences can be examined in a single application without restriction. Applicants contend that there would be no additional search burden on the Examiner because each search relating to macrophage inflammatory protein 3-alpha (SEQ ID NO:3) would necessarily identify all of the art relating to all of the sequences recited in claim 1.

Applicant's arguments have been fully considered, but are not found persuasive because as argued in the previous Office Action filed November 7, 2003, the examination of multiple short sequences of SEQ ID NO:3 would require a separate and distinct search from that of the originally elected claims to compounds targeted to SEQ ID NO:3. As argued in the previous Office Action, compounds targeted to each of the sequences recited in claim 1 is considered to be structurally independent and distinct, even though they each target SEQ ID NO:3, because compounds targeted to each of theses sequences has a unique nucleotide sequence, distinct from the full length of SEQ ID NO:3 and distinct from each other. As further argued in the previous Office Action, a new, separate, and distinct search would be required for each of these target regions, separate from the search of SEQ ID NO:3 and a search and examination for each of these target regions would be unduly burdensome on the Patent and Trademark Office. Therefore, for search and examination purposes, one region is considered to be reasonable.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1 and 2 were rejected under 35 U.S.C. 102(a) as being anticipated by Schlegel et al. [WO/01/42467]. **This rejection is withdrawn** in view of Applicants amendment to the claims to recite, "a compound 8 to 50 nucleobases in length targeted to a 3'-untranslated region of a nucleic acid molecule encoding macrophage inflammatory protein-3 (SEQ ID NO:3)".

Claims 1 and 2 were rejected under 35 U.S.C. 102(b) as being anticipated by Hromas, R. [U.S. Patent No. 6,096,300]. **This rejection is withdrawn** in view of Applicants amendment to the claims to recite, "a compound 8 to 50 nucleobases in length targeted to a 3'-untranslated region of a nucleic acid molecule encoding macrophage inflammatory protein-3 (SEQ ID NO:3)".

Claim Rejections - 35 USC § 103

Claims 1, 2, 4-10 and 12-14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schlegel et al. [WO/01/42467] and Hromas, R. [U.S. Patent No. 6,096,300] in view of Baracchini et al. [U.S. Patent No. 5801154] and Fritz et al. (Journal of Colloid and Interface Science, 1997 Vol. 195:272-288). **This rejection is maintained** for the reasons of record set forth in the previous Office Action, filed December 23, 2002.

Applicants argue that at the outset, the claims have been amended to recite specific regions within the sequence of macrophage inflammatory protein 3-alpha for targeting of antisense compounds, said regions not taught in the cited references. Applicants argue that none of the primary references teach or suggest the claimed antisense compounds and when considered either alone or when combined, the primary references fail to teach the limitations of the amended claims. Applicants argue that nowhere do the references teach or suggest the use of antisense compounds targeted to specific regions of human macrophage inflammatory protein 3-alpha as now claimed. Applicants also argue that Baracchini et al. teach modifications to antisense oligonucleotides to enhance activity, but do not teach or suggest the use of antisense compounds targeted to macrophage inflammatory protein 3-alpha. Applicants further argue that

Fritz et al. disclose cationic polystyrene nanoparticles as carrier systems for antisense compounds in general, but do not teach or suggest the use of antisense compounds targeted to macrophage inflammatory protein 3-alpha.

Applicant's arguments have been carefully considered but are not considered persuasive because the criteria for a 103 rejection is based on three factors: (1) obviousness (2) motivation and (3) expectation of success. In totality, the references render the instant application obvious and demonstrate that one of ordinary skill in the art would have been motivated and expected success in making and using the current invention at the time of filing. As argued in the previous Office action filed December 23, 2002, it would have been obvious to one of skill in the art to make antisense oligonucleotides targeting macrophage inflammatory protein 3-alpha (MIP-3α) since the sequence of macrophage inflammatory protein 3-alpha was known in the art at the time of filing and it was well known to make antisense nucleic acids to known sequences to probe for the function of a specific gene. As further argued in the previous Office Action, one of ordinary skill in the art would have been motivated to inhibit the expression of MIP-3α since the prior art has taught that Exodus MIP-3α is a chemokine that regulates mononuclear chemotaxis, which is important in neoplasia. As further argued in the previous Office Action, one of ordinary skill in the art would have had a reasonable expectation of success in making a compound 8 to 50 nucleobases in length targeted to macrophage inflammatory protein-3 since Baracchini et al. teach how to make antisense oligonucleotides, 8 to 50 nucleobases in length, to any target gene. As further argued, one of ordinary skill in the art would have been motivated to modify the antisense oligonucleotides since the prior art has taught the desirability of such modified oligonucleotides are often preferred over native forms because of enhanced cellular uptake,

enhanced affinity for nucleic acid target, increased stability in the presence of nucleases and the exhibition of high colloidal stability with low toxic side effects as required for biological experiments (Baracchini et al. and Fritz et al.).

Further, regarding a compound 8 to 50 nucleobases in length targeted to a 3'-untranslated region of a nucleic acid molecule encoding macrophage inflammatory protein-3 (SEQ ID NO:3) as now recited in claim 1, and Applicant's arguments that none of the cited references teach specific regions within the sequence of macrophage inflammatory protein 3-alpha for targeting of antisense compounds. The 3'-untranslated region of a nucleic acid molecule encoding macrophage inflammatory protein-3 (SEQ ID NO:3) is explicitly taught by Hromas et al. (see attached sequence alignment at nucleobases 1-60). Baracchini et al. teach the design of antisense oligonucleotides that can specifically hybridize with a 3'-untranslated sequence of a target gene (see column 9, lines 6-67 and column 10, lines 1-25 and Table 1). Therefore, one of ordinary skill in the art would have been motivated to make an antisense compound targeting a specific region, such as the 3'-untranslated region of a nucleic acid molecule encoding macrophage inflammatory protein 3-alpha, because it is well known in the art to target different sites within a gene for the oligonucleotide interaction to occur such that a desired effect (e.g., detection or modulation of expression of the protein) will result. One of ordinary skill in the art would have expected success in making an antisense compound targeting a specific region, such as the 3'-untranslated region of a nucleic acid molecule encoding macrophage inflammatory protein 3-alpha using the sequence taught by Hromas et al. and following the method of Baracchini et al.

Conclusion

Claims 1, 2, 4-10 and 12-14 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Terra C. Gibbs whose telephone number is (571) 272-0758. The Examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
February 9, 2004

SEAN McGARRY
PRIMARY EXAMINER
1635